AMERICAN
Journal of Pharmacy
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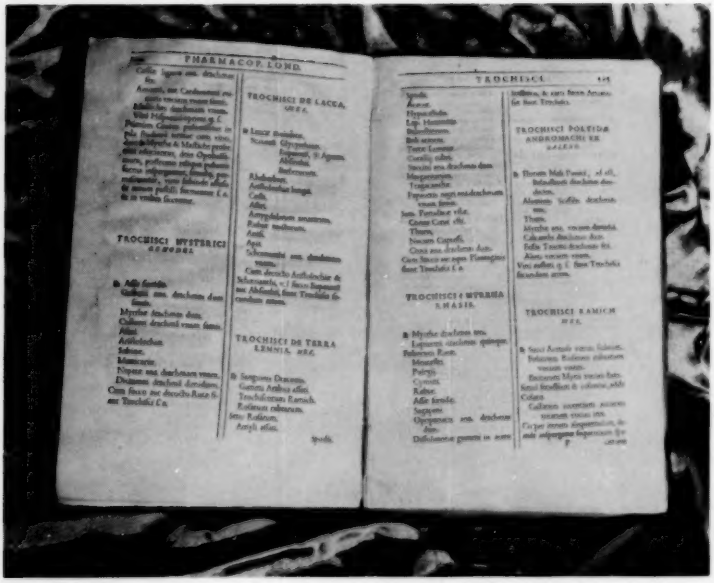
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Since 1825 *March 1957*

American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter March 27, 1937, at the Post Office at Philadelphia, Pa.
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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 129 MARCH 1957 No. 3

CONTENTS

E D I T O R I A L

DANGEROUS DRUG SAMPLES AND POLICE

A PROGRAM was recently announced on the West Coast which, if we understand it correctly, will endeavor to place at various police headquarters a sample board of capsules, tablets, etc., illustrative of each of the so-called dangerous drugs which might be involved in poisoning or criminal cases. Opposition to this plan was registered by one of the officials of the American Drug Manufacturers Association and we think properly so.

On the surface, it would appear that cooperation of this sort between organized pharmacy and the police would be a highly desirable thing and one that might gain for pharmacy a good reputation of assisting public officials in discharge of their duties. A more critical and careful examination of this plan, however, would bring to light a number of potential hazards which, if they were allowed to transpire, might do irreparable damage to pharmacy and to its public and professional relations.

We do not presume to know all of the bases for the objections to this plan by the drug manufacturers but it does not take too much imagination to picture some of them.

In the first place, the identification of a drug purely on the basis of its shape, size, and color is unscientific and hazardous, to say the least. While it is a common belief on the part of the layman that any pharmacist or physician can identify a drug simply by looking at a capsule or tablet, it is rarely possible to do so with any certainty. To use any such snap method as a basis for the selection of an antidote for a poison or the institution of police action seems inconceivable. This, however, is not the worst aspect of any such program. Many persons, entirely innocent of any wrongdoing and surely not drug addicts, make it a practice to carry on their person several tablets or capsules of a drug prescribed by their physician although they are not in the prescription container. We can well imagine the fate of such innocents should they suffer some injury or be taken ill on the street or in a public place. Rather than receiving the attention of a physician, they might well wind up in a prison cell with a *prima-facie* case of drug addiction being placed against them on the basis of the capsules or tablets found in their pockets.

While the police are well-intentioned public officials, it is expecting too much of them to understand all of the intricate problems surrounding the use and misuse of drugs. We have ourselves seen some excellent evidence of typical police methods wherein pharmacy students who were guilty of nothing more than having some physician's samples of drugs in their possession—and these not dangerous—were incarcerated for the night on the suspicion of being drug addicts. Such is the kind of performance that can be expected by officers who have no scientific or technical training whatsoever.

The misuse of drugs is without question a serious problem but it is often magnified beyond its true proportions by a lurid press. There is the further fact that the great bulk of criminal cases involving drugs shows that the drugs did not originate in legitimate pharmaceutical channels. For example, it is somewhat of a paradox that the Harrison Act and its regulations impose very rigid rules on the manufacturer, pharmacist, and physician and, yet, the amount of narcotics getting into the hands of addicts through these channels is almost negligible. It happens to be easy to regulate and control legitimate purveyors of drugs but it is not these who are usually at fault.

While we feel sure that the suggestions made to assist the police in the manner described were made in good faith and in an honest desire to be helpful, we cannot but question the wisdom of such a program.

On the other hand, the establishment of Poison Information Centers under the auspices and supervision of the health professions is a program which all can endorse. Such organized effort to expedite treatment of persons suffering from drug and chemical poisoning can go far in reducing deaths from this cause without placing the responsibility in the hands of police and others who are not qualified for such work.

L. F. Tice

THE PUBLIC HEALTH PROBLEM OF ACCIDENTAL POISONING *

By Bernard E. Conley †

YOU are all aware of the growing attention which is being given to accidental poisoning as an important public health topic. This is not a new problem. However, in this era of preventive medicine accidental poisoning takes on a new and growing importance as a cause of avoidable disease.

Poisonings are not among the leading causes of death; nevertheless they represent a significant proportion of those fatalities that can be prevented. The vast majority of deaths every year are due to conditions of advancing age such as heart disease, cancer and arteriosclerosis for which we have no cure. On the other hand, we've made tremendous strides in decreasing mortality in many conditions where drugs are effective. Today, infectious diseases such as diphtheria, whooping cough, pneumonia and smallpox are no longer among the leading causes of death. This is due to the development of specific immunization procedures and the discovery of remedial agents such as the sulfa drugs and the antibiotics. Unfortunately, we have experienced no comparable improvements in accident prevention. There has been no significant change in the over-all frequency of fatal injuries from chemicals. Consequently, the relative importance of poisoning as a cause of preventable disease has increased tremendously in recent years.

Extent of Poisoning

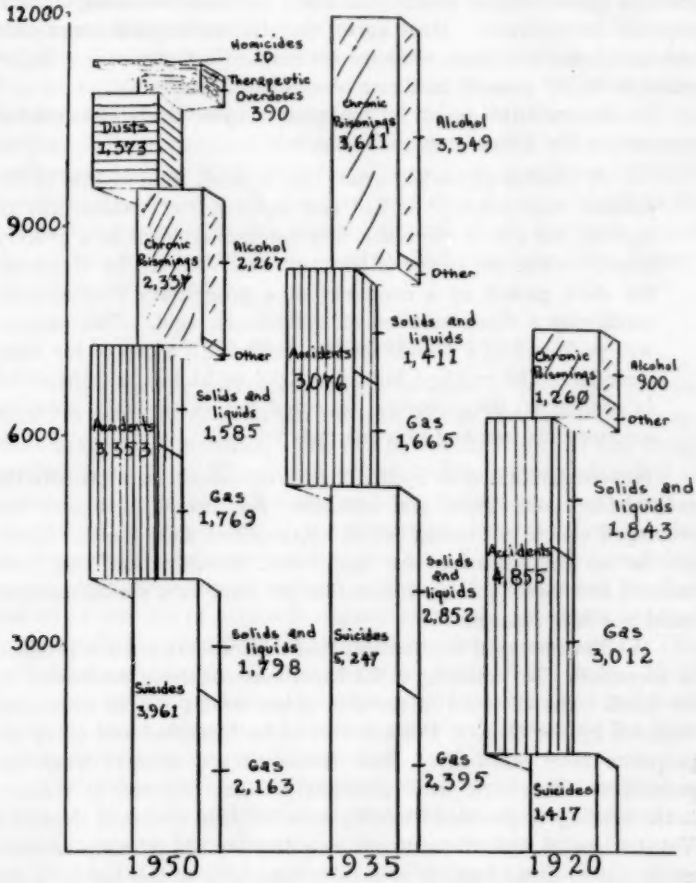
The magnitude of the poisoning problem can be seen from the first figure. You will observe that nearly 12,000 persons lost their lives from accidental and intentional exposure to harmful chemicals in 1950. One-half of these fatalities were classified as unintentional poisonings. By this I mean deaths due to accidents, medical misadventure and occupational exposure. The relatively static position of poison fatalities and particularly accidental poisonings for the past

* Presented before the Annual Meeting of the National Drug Trade Conference, Hotel Gramercy Park, New York, N. Y., December 3, 1956.

† Secretary, Committee on Toxicology, American Medical Association.

generation is evident from Figure I. For this and other compelling reasons, agitation has developed in various quarters to combat this problem. Unfortunately, we have little organized research and no organized campaign for funds to study the causes and prevention of poisoning as have been undertaken for other worthy medical causes.

FIGURE I



DEATHS DUE TO POISONS IN THE UNITED STATES

There is another reason for the growing interest in the public health aspects of accidental poisoning. It is the concern over the increasing number of chemical products containing agents which are recognized in industry as having hazardous properties. The Committee on Toxicology estimates there are over one-quarter million brand-name items available for use on the farm, in industry and in and around the home. The toxicity of the ingredients in many of these products poses a major health problem if users are unaware of their potential harmfulness. Most agree that the widespread casualness with which many of these products are handled and stored is a major influence in the present incidence of accidental poisoning.

To illustrate this point, let me quote a case which was recently reported to the Committee on Toxicology:

> A Florida physician wrote that a small child of one of his patients was severely burned and suffered the possible loss of sight in one eye as the result of a needless accident in a grocery store. While the mother's attention was diverted by shopping, the child picked up a container of a proprietary rust-remover containing a dilute solution of hydrofluoric acid. This product was packaged in a plastic squeeze bottle with a cap of the same material. The cap had been dislodged or broken and the child, in picking up the container, squeezed the plastic bottle spraying acid into his face and into one eye.

Anyone familiar with hydrofluoric acid burns, can appreciate the excruciating pain, rapid and extensive destruction of tissue, and prolonged course of healing which accompanies such burns. There can be no compensating the injury and disfigurement this child suffered and there is no assurance that the same or a similar accident could not happen again.

We have no legal requirement that the contents of such products be identified. No warning of its hazardous nature is demanded for the label. The chemical in question is not among the 12 substances required by the Caustic Poisons Act to be identified and carry appropriate label warnings. Rust removers are neither drugs nor pesticides. Therefore, such products are not required to conform to the labeling provisions of existing laws for these classes of chemicals. Yet, the use of hydrofluoric acid as a laundry aid is fairly common as shown by other reports of injury, especially to the hands, which we have since received.

As this case of injury suggests, risks are present even in the most commonplace situations and the hazards are often subtle and not always comprehensible. The consequences of poisoning are most evident in the statistics on the incidence and cost of non-fatal injuries from chemicals. The relationship of fatal to non-fatal poisonings has been compared to the exposed and hidden parts of an iceberg. That is, for every fatality, an estimated 100 to 250 non-fatal injuries occur. These figures indicate that there is more to the poisoning problem than appears above the surface.

This is particularly true with regard to the cost of poison injuries. For example, welfare agencies estimate that it costs $8,000 to cover hospitalization and surgical treatment of a child with stricture of the esophagus from ingestion of a corrosive, such as lye. Compensation settlements in New York State for silicosis average well over $14,000 per case. The loss of a life, however, is of even greater expense to the productive resources of this country because of the economic loss of the victim's working years to society. Unfortunately, these aspects are often overlooked.

Drugs as a Cause of Poisoning

Before turning to current efforts to improve poisoning prevention, I would like to point out the special contribution which drugs make to mortality statistics. You will note from Figure II that drugs produce from 20 to 25 per cent of the fatal poisonings classified as accidents and suicides. If fatalities from therapeutic overdoses and drug addiction are considered, the proportion of accident fatalities due to drugs would be considerably greater. Significantly, medicinal agents constitute a minor fraction (1/10 to 3/10 per cent) of the total annual production of synthetic organic chemicals, yet drugs produce from one-fifth to one-third of the fatal accidental poisonings. This is a disproportionately high incidence of deaths from drugs. It is hard to escape the conclusion that widespread casualness and ignorance about the toxic properties of familiar medicinal agents are the basic factors underlying this persistently high death toll.

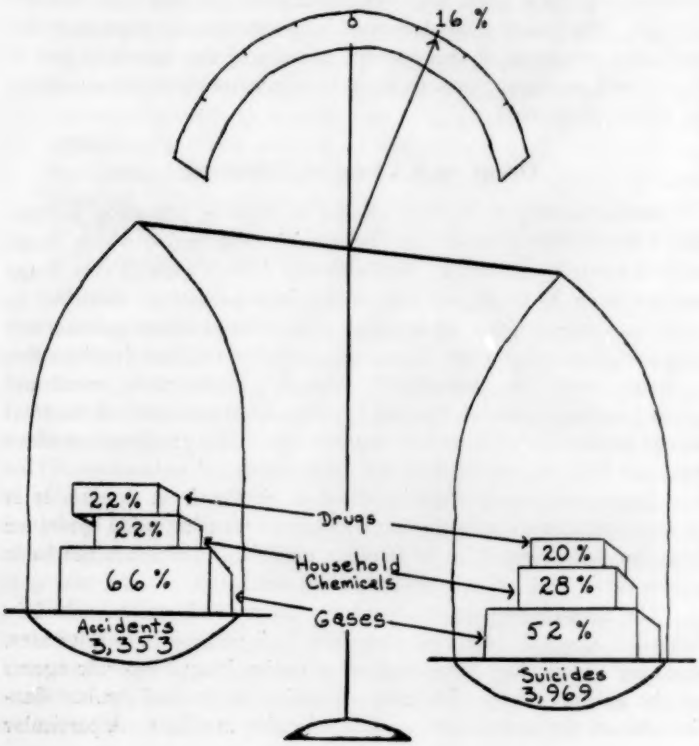
The drugs which most frequently cause death are tabulated in Table I. You will note that medicines such as aspirin, barbiturates, bromides, opium derivatives and other analgesic and soporific agents are the leading causes of accidental deaths due to medicinals. Barbiturates are the commonest cause of poisoning in adults. A particular

danger of the barbiturates is the mental dulling and disorientation which may accompany even a single dose. As a result the patient may take additional doses and intoxication may ensue. Concurrent use of alcohol also increased the chances of serious and even fatal poisoning.

Therapeutic overdoses which are not the result of medical error also occur more frequently than is commonly suspected. Aspirin poisoning in children induced by over-liberal administrations of this drug by parents has been often reported. Another example is the case of the housewife inspired to self-medication by a "Nutrition

FIGURE II

ACCIDENTAL VS. SUICIDAL POISONING
1950



commentator" who suggested vitamin A for "alleviating dry throat and as a prophylactic for colds." Following this advice, the patient instituted a self-prescribed regimen of 600,000 units per day and doubled or tripled this amount when she felt a cold coming on. This is from 100 to 500 times the average daily adult requirement. Eighteen months later the patient developed frank symptoms of poisoning which required hospitalization.

Accidental deaths due to mistaken ingestion of externally applied preparations, such as liniments, are not infrequent. A growing danger with our increasing older population is the mistaken use of the wrong medicine, particularly at night. The decreased acuteness of taste and smell, and the dimming of vision which accompanies old age undoubtedly contributes to this type of drug poisoning. The mistaken ingestion of the wrong medicine by an older person is illustrated by the following case:

> An elderly man had the habit of drinking medicine directly from the bottle. One night, apparently without benefit of the bathroom light, he reached for his tonic, but picked up a similarly sized bottle of a proprietary liniment. As was his usual habit, he put the bottle to his lips and swallowed some liniment. A physician was called and the patient was induced to vomit. A half an hour later, the old man complained of numbness of the tongue and extremities and became seriously ill. An ambulance was called but the patient died on admission, of aconite poisoning.

The comparative frequency of accidental drug poisoning for various age groups is tabulated in Table II. This table presents a breakdown of the miscellaneous category of drug deaths recorded in the previous table. You will observe that a variety of agents are involved and mortality appears to be fairly evenly divided between pre-school age children and those 5 years of age and over. This distribution is misleading since the incidence of poisoning by aspirin and other salicylates for both age groups are not considered.

Aspirin poisoning has been shown to be most frequent in the very young. A Committee on Toxicology report (JAMA *158*:831, July 9, 1955) pointed out that salicylate poisoning predominately occurs in small children. In 1950, for example, 99 fatalities were reported for salicylates such as aspirin, oil of wintergreen and sodium salicylate. Approximately 80 per cent of these deaths occurred in children under 5 years of age.

TABLE I

DEATHS FROM ACCIDENTAL POISONING

Substance	Total (All ages)
Accidental poisoning by solid and liquid substances (E870-E888)	1,584
Morphine and other opium derivatives	22
Barbituric acid and other derivatives	409
Aspirin and salicylates	99
Bromides	14
Other analgesic and soporific drugs	109
Sulfonamides	4
Strychnine	23
Belladonna, hyoscine, and atropine	2
Other and unspecified drugs	59
Noxious foodstuffs	18
Alcohol	246
Petroleum products	112
Industrial solvents	34
Corrosive aromatics, acids, and caustic alkalies	78
Mercury and its compounds	23
Lead and its compounds	61
Arsenic and antimony, and their compounds	58
Fluorides	9
Other and unspecified solid and liquid substances	204
Accidental poisoning by gases and vapors (E890-E895)	1,769
Utility (illuminating) gas	1,012
Motor-vehicle exhaust gas	351
Carbon monoxide gas	251
Cyanide gas	9
Other specified gases and vapors	105
Unspecified gases and vapors	41

Table adapted from data in Vital Statistics—Special Reports, National Summaries, Deaths and Crude Death Rates for Each Cause, by Race and Sex: United States 1950, Volume 37, No. 6, February 16, 1953.

TABLE II

DEATHS FROM ACCIDENTAL POISONING BY "OTHER AND UNSPECIFIED DRUGS": UNITED STATES, 1950

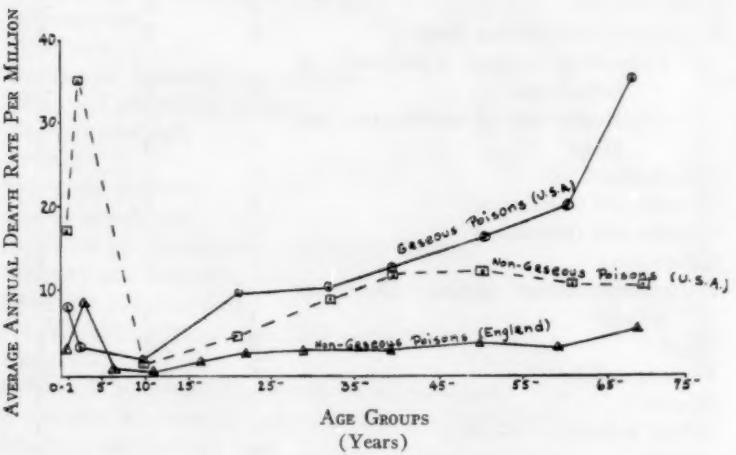
Substance	Total (All ages)	4 yrs. and Under	5 yrs. and Over
Total	59	27	32
Antihistamine	4	3	1
dimenhydrinate (Dramamine)	1	1	—
Neoantergan	1	1	—
Other	2	1	1
Cold tablets	2	2	—
Aminophylline	2	2	—
Barbiturate and another drug	8	5	3
Vinbarbital sodium (Delvinal) & belladonna	1	1	—
Other mixtures of barbiturates and drugs	7	4	3
Camphorated oil	1	1	—
Cascara and belladonna	1	1	—
Codeine and chloroform	1	1	—
Colchicum	1	—	1
Dextroamphetamine sulfate (Dexedrine sulfate)	1	1	—
Ergot	2	1	1
Ferrous sulfate	1	1	—
Insulin	3	—	3
Iodine, iodoform, iodophen	4	1	3
Peyote	2	1	1
Veratrum Viride	4	3	1
Other drugs and hormones	6	—	6
Epinephrine	1	—	1
Desoxycorticosterone	1	—	1
Digitalis	1	—	1
Neostigmine (Prostigmine)	1	—	1
Thiouracil, thyroid extract	2	—	2
Drug, tablets, overdose of medicine	16	4	12

Note.—Deaths assigned to category E878, Sixth Revision of International Lists.

That the pre-school age child is more susceptible to accidental poisoning is evident from Figure III. This Figure compares the annual death rate from accidents in England and the United States for various age groups. You will note that for most age groups the death rate in the United States is two to four times that of Great Britain. For pre-school children, it is six times as high as the death rate in England. The reason for this higher death rate in the United States is attributed to the greater availability of drugs and other chemicals capable of causing harm.

FIGURE III

COMPARISON OF ACCIDENTAL POISONINGS IN ENGLAND AND THE UNITED STATES FOR A TEN YEAR PERIOD
1940-1949



Poisoning Prevention Programs

The principal major efforts to combat accidental poisoning are centered in two independent but related movements; namely, the establishment of poison information centers in various cities and the development of chemical label laws for products not now so regulated. Both movements are receiving support at both the local and national levels. They have also survived the initial enthusiasm and subsequent diminution of interest which accompany all new undertakings. Both undertakings have already a record of accomplishment which I will summarize.

The first community poison information center was established in Chicago in the fall of 1953 under the sponsorship of the Illinois Chapter of the American Academy of Pediatrics. It was a cooperative venture of the local health department, the five medical colleges, the major Chicago hospitals and the state toxicological laboratory. Representatives of the American Medical Association, the Federal Food and Drug Administration and the National Safety Council also participated in the organization. Since then a number of other cities have developed generally similar centers.

We have been advised of the existence of poison information groups in nearly fifty cities, 80 per cent of which are presently offering some type of service. The manner of organizations of these centers varies with the community. In at least three large metropolitan areas, poison information facilities have been organized under the auspices of the city or county health department whose personnel provide staff service. In one other city, this type of arrangement was initially undertaken but is no longer maintained. In three additional cities, the poison information center is maintained by the local medical society. Schools of medicine and their affiliated research centers furnished poison information services in five additional localities while in the remaining cities, centers were established in local hospitals by private physicians who volunteered part-time service. Most of the centers are experiencing problems peculiar to activities that depend on voluntary and part-time help. There is hope that centralizing some of the duties associated with compiling information and keeping records might ease the growing pains of these groups. The feasibility of establishing a central agency to provide information to centers and to tabulate their poisoning cases is presently being investigated. A steering committee to develop a national poison information center, possibly within a federal government agency has been actively working towards this goal.

The poison centers have demonstrated that they can fill a very definite need. In addition to supplying information and compiling injury reports, they are helping to create awareness of accidental poisoning in the public as well as the medical profession. Poison centers and their affiliated hospitals also provide unique opportunities for certain types of clinical studies. For example, a national cooperative project for the study of the treatment of kerosene poisoning has been initiated under the auspices of the A. M. A. Committee on Toxicology, the American Academy of Pediatrics and the American

Public Health Association. Over 25 poison centers and their affiliated hospitals are participating in this program. This study will evaluate such diverse aspects as the use of anti-inflammatory agents in treatment of kerosene poisoning and means for determining blood levels of absorbed petroleum distillates.

The demand for label laws for so-called "household chemicals" is the second development of national importance. Recently the Board of Trustees of the American Medical Association authorized the Committee on Toxicology to develop, in conjunction with other interested and informed groups, a uniform chemical label law. The proposed legislation is intended to cover the existing gap in the pattern of regulations requiring precautionary labeling and the identification of hazardous ingredients.

The mandate to the Committee on Toxicology to spearhead this legislative project is not without precedent. A generation ago, another A. M. A. Committee drafted a Model Lye Law. Through the efforts of this Committee and state medical associations, legislation was considered both locally and nationally. This eventuated in passage of the Federal Caustic Poisons Act of 1927.

The proposed Uniform Chemical Label Law is directed at many products now sold in drug stores such as lighter fluid, cleaning solvents, maintenance and decorating supplies and the variety of other household and commercial chemicals not now so regulated. The advice and assistance of pharmacy groups will be sought in this enterprise.*

* A resolution of the National Drug Trade Conference to cooperate with the AMA on the public health problem of accidental poisoning has since been announced (Author/Editor).

ERRATUM

The graph plotting the solubility of sodium bromide in hydroalcoholic solutions presented as Figure I on page 66 in the February issue reversed the legends given. The ordinates should be % w/v sodium bromide and the abscissae % v/v C_2H_5OH.

STUDIES ON THE EFFECTS OF ASCORBIC ACID AND HESPERIDIN UPON HISTAMINE-INDUCED GASTRIC ULCERS IN GUINEA PIGS *

By G. Victor Rossi, Elias W. Packman and Morton E. Goldberg

IN recent years much experimental and clinical evidence has been advanced to support the concept of synergism existing between ascorbic acid and the bioflavonoids in the maintenance of capillary integrity. The stimulating contention has been offered that there are no disease states which could not be benefited by assuring proper capillary strength. Certainly the importance of the vascular component in the pathomechanism of peptic ulcer is widely recognized.

On this basis a study was designed to evaluate the ability of ascorbic acid, hesperidin and the combination of ascorbic acid and hesperidin to prevent or modify depot-histamine induced gastric ulcers in guinea pigs. It was further intended that this investigation would provide additional data on the synergism between ascorbic acid and bioflavonoids which has been demonstrated in many other biological systems.

Method

English smooth hair male guinea pigs of 250 to 350 grams body weight were employed throughout this study. All animals were maintained in individual cages in constant temperature quarters and allowed free access to Rockland Guinea Pig Diet and tap water.

The investigation was performed in two parts. The initial study was concerned with the effect produced by forced oral feeding of ascorbic acid and hesperidin upon the development of gastric ulcers induced by the concomitant administration of histamine. For this phase of the study, four experimental groups were established as follows:

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* Received from the LaWall Memorial Laboratory of Pharmacology and Biochemistry, Philadelphia College of Pharmacy and Science.

This study was supported in part by a research grant received from the National Drug Company, Philadelphia, Penna.

Group I. Control (Distilled Water)
Group II. Ascorbic Acid Treated
Group III. Hesperidin Treated
Group IV. Ascorbic Acid and Hesperidin Treated

Freshly prepared aqueous suspensions of the test materials were given by intraesophageal administration twice daily, in the morning and in the evening. Each dose contained 50 mg. of each test substance assigned to the respective group.

Gastric ulcers were produced according to a modification of the method of Hay et al. (1). All animals received a daily intramuscular injection (into the back musculature) of 1.0 ml./Kg. depot histamine. The depot histamine was prepared by suspending 25.0 mg. of thoroughly desiccated histamine diphosphate in 1.0 ml. of a mixture containing beeswax and mineral oil in a ratio of 1:3.4. Upon injection the mixture solidifies forming a depot which requires about 24 hours for complete absorption.

All surviving guinea pigs were killed and autopsied ten days after treatment was initiated. The stomach and duodenum of each animal were examined, for evidence of mucosal damage, by impartial judges. Animals which died during the experimental period were autopsied as soon after death as possible. The degree of mucosal damage was rated, and the index of mucosal damage was calculated according to the arbitrary standards and formula described by Harrisson et al. (2), which were patterned after the criteria devised by Pauls et al. (3). The grading system employed was as follows:

Degree of Mucosal Damage

0 = Normal stomach (no apparent gross damage)
1 = Doubtful damage
2 = Occasional or moderate hemorrhagic lesion
4 = Pronounced hemorrhagic lesion or damage to mucosal wall
6 = Well defined damage to mucosal wall
8 = Non-penetrating ulcer
10 = Penetrating or perforated ulcer

$$\text{Index of Mucosal Damage} = \frac{\text{Mean Degree of Mucosal Damage} \times \text{Percent of Group Evidencing Damage}}{100}$$

The second phase of the study was designed to demonstrate the difference in effects obtained with forced oral feeding of the test materials as compared to the incorporation of ascorbic acid and hesperidin in the daily diet of the experimental animals. Whereas in the initial investigation ascorbic acid and hesperidin were not administered until histamine was injected, in the second phase the test materials were added to the diet two weeks before attempts were made to induce gastrointestinal ulceration.

Three additional groups were established for this latter phase of the experiment:

Group V. Control
Group VI. Ascorbic Acid and Hesperidin Treated (Low Level)
Group VII. Ascorbic Acid and Hesperidin Treated (High Level)

On the basis of preliminary studies which determined the amount of milled Guinea Pig Diet consumed by each animal per day, ascorbic acid and hesperidin were uniformly incorporated in the diet in a concentration calculated to provide 10 mg. of each factor per day in Group VI (Low Level) and 20 mg. of each factor per day in Group VII (High Level).

Induction and evaluation of mucosal damage were performed as described for the initial study.

Results

The percent of animals manifesting grossly visible damage to the gastrointestinal mucosa, the mean degree of mucosal damage and the index of mucosal damage are compared in Table I for each experimental group receiving intraesophageal injections of the test materials, and in Table II for those groups ingesting ascorbic acid and hesperidin in the milled ration.

The index of mucosal damage is considered the most valid criterion for evaluation of the data obtained since it takes into consideration both the degree and incidence of mucosal damage. It should be noted that the lesser the index of mucosal damage, the greater is the protection offered by the treatment under evaluation.

TABLE I

GASTRIC ULCER STUDY

SUMMARY OF THE DEGREE OF MUCOSAL DAMAGE IN GUINEA PIGS

	Group I. Distilled Water	Group II. Ascorbic Acid	Group III. Hesperidin	Group IV. Ascorbic Acid + Hesperidin
No. of Animals Manifesting Mucosal Damage	18/20	18/20	17/20	14/20
No. of Animals in Group				
Percent of Animals Manifesting Mucosal Damage	90	90	85	70
Mean Degree of Mucosal Damage	7.2	4.1	6.0	3.6
Index of Mucosal Damage	6.48	3.69	5.10	2.52

During the test period each animal received depot-histamine, 25 mg./kg. intramuscularly, once daily; and distilled water (Group I.), ascorbic acid 50 mg. (Group II.), hesperidin 50 mg. (Group III.), or ascorbic acid 50 mg. and hesperidin 50 mg. (Group IV.) administered intraesophageally, twice daily.

Discussion

Both the mean degree of gastric mucosal damage and the index of mucosal damage were reduced in all treated groups of guinea pigs as contrasted to the non-treated (control) groups. Considering those animals receiving forced oral medication, ascorbic acid administered alone (Group II) appeared to have a greater inhibitory effect against histamine-induced gastrointestinal erosion than an equivalent amount of hesperidin alone (Group III). The concomitant administration of both ascorbic acid and hesperidin (Group IV) provided substantially greater protection than either ascorbic acid or hesperidin alone.

Because of the many known and unknown variables inherent in such a study, it is not possible to statistically validate the data obtained. Nevertheless, it is our opinion that the results indicate a definite synergism between ascorbic acid and hesperidin in the prevention of histamine-induced gastric mucosal damage in guinea pigs.

TABLE II

GASTRIC ULCER STUDY

SUMMARY OF THE DEGREE OF MUCOSAL DAMAGE IN GUINEA PIGS

	Group V. Control	Group VI. Ascorbic Acid + Hesperidin	Group VII. Ascorbic Acid + Hesperidin
No. of Animals Manifesting Mucosal Damage	16/17	15/17	12/17
No. of Animals in Group			
Percent of Animals Manifesting Mucosal Damage	95.3	88.2	70.6
Mean Degree of Mucosal Damage	5.67	3.50	2.32
Index of Mucosal Damage	5.40	3.09	1.64

Ascorbic acid and hesperidin incorporated in diet for 14 days prior to and including test period in concentrations calculated to provide 10 mg. of each factor per day in Group VI., and 20 mg. of each factor in Group VII. Dose received per day based on average daily food intake of 30 Gm. During test period, all animals received depot-histamine 25 mg./kg. intramuscularly, once daily.

Gastrointestinal ulceration is a complex phenomenon which undoubtedly involves numerous factors in addition to the many which have been characterized. The histologic picture of histamine-induced gastric ulcers in guinea pigs is claimed to be comparable to that observed in human peptic ulcers (3). However, it must be emphasized that some investigators consider the pathomechanism of gastrointestinal ulcers produced either by depot-histamine or pyloric ligation (4) to be unrelated to those observed in the clinic.

In this study, the greatest protection against histamine-induced gastric lesions was obtained when ascorbic acid and hesperidin were incorporated into the diet of the experimental animals for two weeks prior to and during the time the ulcerogenic agent was administered (Group VII). It should be noted that greater protection was provided by 20 mg./day each of ascorbic acid and hesperidin included in the diet than by 5 times that amount of those substances administered by forced oral feeding. Two factors undoubtedly contributed to the greatly reduced incidence and degree of gastric damage: (a)

pretreatment with these nutritional substances increased capillary resistance to histamine damage, and (b) ingestion of small amounts of these substances at frequent intervals throughout the day maintained capillary strength at a higher level than intermittent administration of large doses of these rapidly excreted compounds.

Although the mode of action of ascorbic acid and hesperidin in reducing gastric mucosal damage remains largely obscure, the burden of experimental evidence indicates that they function to maintain capillary integrity in the presence of histamine insult. This contention is supported by recent work (5) which indicates that the vascular component of the gastric response to histamine plays a greater role than the secretory component in the genesis of histamine-induced ulcers.

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DRUG INFORMATION SOURCES *

(Great Britain and The Netherlands)

GREAT BRITAIN

Pharmaceutical Society of Great Britain. The British Pharmaceutical Codex 1954. London, Pharmaceutical Press, 1954. 1340 pp. 63s.

The *British Codex* is a reference work on all drugs included in the *British Pharmacopoeia* and many not in the *Pharmacopoeia;* it is also a book of standards for drugs not included in the *Pharmacopoeia.* Monographs on drugs (Part I) are entered alphabetically under *British Pharmaceutical Codex* name and provide alternate names (official or generic, Latin, Latin abbreviation, synonyms), chemical composition, structural and empirical formulas, tests and standards, solubility, action, antidotes, uses, incompatibility, dosage, method of administration and directions for sterilization and storage. Lists of preparations to be found in the Formulary (Part VI) or in the British Pharmacopoeia are appended. Other sections contain monographs on biological products, human blood preparations, surgical ligature and surgical dressings. Proprietary names are not included in the monographs of the *Codex;* lists referring from *Codex* name to brand name and from brand name to *Codex* name are published as a pocket supplement. The general alphabetic index includes all drug names found in the text of the *Codex;* it is unique in its inclusion of chemical names.

Pharmaceutical Society of Great Britain. The Extra Pharmacopoeia (Martindale), incorporating **Squire's Companion.** 23d ed. London, Pharmaceutical Press, 1952-1955. 2v. (1352, 1501 pp.) (55s., 57s./6d.)

This comprehensive two-volume reference work presents the latest developments in medicine and allied sciences in the form of monographs or abstracts. In Volume 1, monographs on drugs are

* A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

entered alphabetically under the Latinized form of the official name. Volume 2 includes analytical addenda to the monographs in Volume 1 and additional monographs on related subjects of interest in the fields of medicine and public health. Monographs in Volume 1 report description, properties, actions, uses, toxicity, contraindications and dosage of the subject drug and usually of other drugs having the same or related pharmacologic effects; they are documented by brief abstracts of clinical articles from British, American and foreign journals. Emphasis throughout is on *usage* of drugs in specific conditions. Generic and chemical names are included in the monographs and lists of proprietary-name products with their manufacturers are appended. A section listing formulas of proprietary medicines supplied without prescriptions is included in Volume 2, pp. 1408-1433. Official, generic and proprietary names are included in the alphabetic general index.

Index of New Products. London, **The Pharmaceutical Journal.** Cards 4″ x 6″. 42s.

In this card service on ethical drugs of British manufacturers and distributors, products are entered by proprietary name or by common name if no proprietary name is used. Information includes composition, properties, stability and storage, indications and contraindications, toxicity, dosage, references to journal literature, packing and price and manufacturer's name and address. A therapeutic index and a list of cross references from official and common names to proprietary names are published periodically in a booklet.

"The Compend"; a Compendium of Ethical Proprietaries Used in Medicine and Pharmacy, compiled by William Hetherington. Bristol, John Wright, 1955. 676 pp. 32s/6d.

This pocket-size handbook provides essential details about more than 2500 drug products in active use in Great Britain. Monographs are arranged alphabetically; each gives name of product, poison schedules (if any), name of manufacturer or distributor, composition, therapeutic indications, dosage, method of administration, contraindications, forms and packing. Additional sections provide a list of names approved by the British Pharmacopoeia Commission with their

chemical and proprietary names, a list of international units and standard values, a list of chemical and common names cross referenced to the names of preparations in which they are found, a therapeutic index and a list of manufacturers with their addresses.

Pharmacopoeia, ed. by G. E. Hesketh. London, Butterworth, 1953. 542 pp. (A part of the **British Encyclopedia of Medical Practice.** 2d ed. 1950-1953) 65s.

Gives composition, action and uses, pharmacology, indications, dosage and administration, application, side effects and packing for all drugs listed in the *Encyclopedia.* A condition index is also included.

Pharmaceutical Society of Great Britain. The Pharmaceutical Pocket Book. 16th ed. London, Pharmaceutical Press, 1953. 422 pp. 18s/6d.

A pharmacy reference book for the practicing pharmacist. A useful feature is the "Dictionary of Synonyms," pp. 338-416, a list of about 4,000 synonyms, many almost obsolete, "culled from a wide variety of sources over a long period." All synonyms official in the *British Pharmacopoeia* or *British Pharmaceutical Codex* are included, but proprietary names are not included.

The Scottish Chemists' Index of Modern Remedies. 7th series. Glasgow, **Scottish Chemist,** 1954. 88 pp. Approx. $1.00.

A physician's handbook. Sections are arranged alphabetically by indications (Anaesthetics and Local Anaesthetics, Analgesic and Anodyn, Antacids and Digestants, etc.). Drugs are printed in boldface; trade names are used. A brief description of each drug, including composition, action, manufacturer's name and packing, is in the form of continuous commentary. A list of manufacturers with their addresses (mostly English with some Scottish), a supplementary section on sterile injection solutions, tables on single and multiple vitamin preparations and a general alphabetic index to all drug names are also included. Publisher's address: 240 Albert Drive, Pollokshields, Glasgow, S.1; distributed also by H. K. Lewis, London.

Retail Chemist Trade Price List. Current.

A list issued in book form. Information includes name of manufacturer, size of available packs, retail and trade price and Purchase Tax liability for proprietary articles. Supplements are cumulative.

Pharmaceutical Society of Great Britain. The British Veterinary Codex 1953. London, Pharmaceutical Press, 1953. 737 pp. 45s.

The *British Veterinary Codex* is both a compilation of recommended standards for veterinary drugs and a reference work on the actions and uses of these substances. Monographs in Part I are entered alphabetically under *British Veterinary Codex* names and provide alternate names, chemical composition, structural and empirical formulas, tests and standards (or, alternatively, a reference to the *British Pharmacopoeia* or *British Pharmaceutical Codex*), solubility, action and uses, dosage, method of administration, toxicity, incompatibility and directions for sterilization and storage. Names of relevant preparations are listed after most monographs; details of the composition of these preparations are given in the Formulary (Part III). Antisera and vaccines are in Part II and the Appendixes describe tests and methods of assay. Proprietary names are not included in the monographs, but a list cross-referencing *Codex* names and proprietary and trivial names is appended. A therapeutic and pharmacological index is included. The general alphabetic index includes all *Codex*, chemical, trivial and proprietary names.

NETHERLANDS

Koninklijke Nederlandse Maatschappij ter Bevordering der Pharmacie. Codex Medicamentorum Nederlandicus. 2d ed., 2d printing. 's-Gravenhage, De Gebroeders Van Cleef, 1950.

A dispensatory. The 1950 printing is a reprint of the 1942 (2d) edition with corrections and some regulations left out. Further annotations will appear in a later issue of "Drug Information Sources."

Pinkhof en Van der Wielen, Pharmacotherapeutisch Vademecum. 9th ed., edited by A. Th. Knoppens and Prof. Dr. J. Kok. Amsterdam, Centen, 1951. 1017 pp. Hfl. 20.

Gives therapeutic and pharmaceutical details, including indications, action, composition, dosage and literature. In alphabetic order according to official nomenclature, with indexes on subject and product. Manufacturers' names are not given. Publisher's address: D. B. Centen's Uitgeversmaatschappij (NV), Sarphatikade 12, Amsterdam. [Publisher states that the 9th edition is out of print; 10th edition expected to be published winter 1956-1957 at a price of about Hfl. 40.]

Pharmacological and Chemical Synonyms, compiled by E. E. J. Marler. Amsterdam, **Excerpta Medica,** 1956. 85 pp. Hfl. 13.50.

This compilation, which bears the subtitle "A collection of more than 5000 references from the medical literature of the world," was originally developed as a key to the Subject Index of Section *Physiology, Biochemistry and Pharmacology* of *Excerpta Medica.* It consists of an alphabetic list of synonyms used in the literature for drugs with reference to an approved name and a selective alphabetic list of approved names followed by their synonyms. The synonyms are proprietary names, chemical names or experimental numbers representing research compounds; the approved names are official or generic names approved by Pharmacopoeia councils (usually British or U. S.) or chemical names as devised by leading chemical abstracting journals (in the case of compounds other than drugs or drugs to which no such official name has been given). Publisher's address: 111 Kalverstraat, Amsterdam.

Geneeskundig Jaarboekje voor Nederland, edited by Dr. S. A. Westra and J. B. Lenstra. Rotterdam, Van Hengel, 1955. 394 pp. Hfl. 20.

For the general practitioner and specialist. List of dosages of drugs in alphabetic order, with composition and indications. Very complete. Contains drugs which are not in common use. Name of manufacturer is not given.

Therapie Compendium; Receptuur voor de Huisarts, by Henri R. M. de Haan. 5th ed. Amsterdam, Centen, 1952. 650 pp. Hfl. 13.50.

For the general practitioner. In alphabetic order of name of disease or complex of diseases, with index of drug names and "list of specialties" with name of manufacturer. The compendium gives indications about the whole of therapeutic measures to be used, rather than drugs only. [Publisher states that the 5th edition is out of print. 6th edition is to be published by Messrs. L. Stafleu, Stationsweg 10, Leiden.]

Vademecum voor de Praktizerende Geneesheer in Nederland en de Overseese Gebiedsdelen, by T. Eernstman. 12th ed. Utrecht, Oosthoek, 1948. 988 pp. Hfl. 15.50.

Therapeutic guide and drug list for the practitioner in Holland and in overseas possessions. Publisher's address: N. V. A. Oosthoek's Uigeversmaatschappij, Domstraat 1-3, Utrecht. [A new revised edition is in preparation and will be ready in 1957.]

Nederlandse Chemische en Pharmaceutische Producten en Hun Fabrikanten. 3d ed. 's-Gravenhage, Vereniging van de Nederlandse Chemische Industrie, 1956. 385 pp. Hfl. 11.

This directory contains a *Classification of Pharmaceutical Products* (Alkaloids, Anaesthetics and Narcotics, Analgesics, Sedatives, Hypnotics, etc.) and another section, *Lijst van Nederlandse Pharmaceutische Fabrikanten,* which lists manufacturers of products in the various classes. Pharmaceutical specialties are grouped as a class; individual product names are not mentioned. The major sections are a list of chemical and pharmaceutical manufacturers with their addresses and types of products and a listing of bulk chemicals, including medicinals, with their manufacturers. Names of products are usually given in Dutch, French, English, German and Spanish; keys to the Dutch lists are printed in all the other languages, Publisher's address: Javastraat 2, 's-Gravenhage.

Materia Medica Vegetabilis, by E. F. Steinmetz. Amsterdam, The Author, 1954-1955. 3 parts (593 pp.) Hfl. 69.

A compilation of monographs on plant drugs in English, Dutch, German and French. Entries are listed alphabetically under species name. Monograph gives family name, synonyms, description and medicinal action and uses. Five alphabetic indexes to the text are included, the first being a Latin index to all botanic names and the others, indexes to common names in each of the four languages used. Publisher's address: Keizersgracht 714, Amsterdam.

The Committee on Drug Information Sources has the following members:

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Correspondence about "Drug Information Sources" should be directed to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J.

THE SOLUBILITY OF SORBITOL IN HYDROALCOHOLIC SOLUTIONS *, **

By Martin Barr, S. Robert Kohn, and Linwood F. Tice

Abstract

SORBITOL is used widely as an ingredient of many liquid pharmaceuticals such as elixirs and syrups which often contain alcohol as one of their ingredients. Since no information is available from the literature on the effect of alcohol on the solubility of sorbitol, experiments have been carried out and data are reported on the solubility of this substance in hydroalcoholic solutions.

Introduction

Sorbitol is a hexahydric alcohol having the empirical formula $C_6H_{14}O_6$ and a molecular weight of 182.2. It is finding increasing use in various products because of some of the properties it possesses; among these may be mentioned its sweet taste (approximately 60% as sweet as sucrose), humectant action, chemical inertness, relatively high viscosity in aqueous solution, uniformity, and ready availability. It is acceptable as a wholesome ingredient for foods and ingestible pharmaceuticals.

Sorbitol is used widely in the preparation of liquid products such as elixirs and syrups which often contain alcohol as one of their ingredients. Whereas sorbitol is very soluble in water (1), the addition of alcohol to aqueous systems is known to reduce its solubility. Because of its extensive use in hydroalcoholic preparations, it was deemed advisable to study the solubility of sorbitol in such systems. This paper reports on the results of this study.

Experimental

Solubility studies were carried out on sorbitol [1] in hydroalcoholic solutions of various strengths. The sorbitol content was determined

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** Work supported by a research grant from the Atlas Powder Company, Wilmington, Del.

1. Crystalline Sorbitol, Atlas Powder Company.

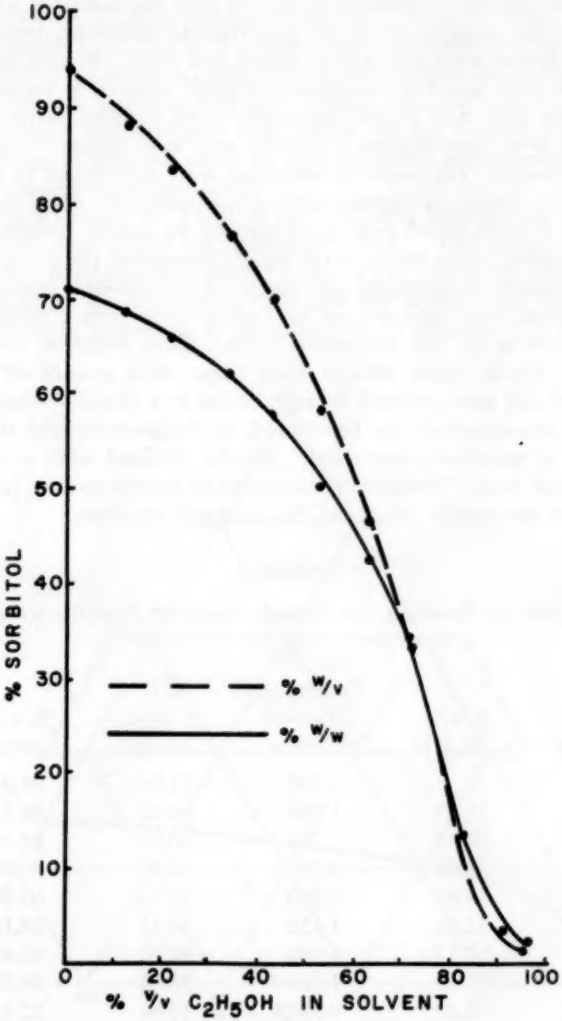

FIG. 1. SOLUBILITY OF SORBITOL IN HYDROALCOHOLIC LIQUIDS AT 25° C.

by a modified T. G. A. Method 47 (2) involving periodic acid oxidation following the evaporation of alcohol from the saturated solution.

For the preparation of the experimental solutions, four-ounce tincture bottles were thoroughly cleaned and dried. Rubber stoppers for these were boiled in a sodium hydroxide solution to remove any impurities and then rinsed thoroughly with distilled water. The stoppers were then washed in alcohol and, once again, rinsed with distilled water. The points of saturation were approached by adding sorbitol to liquids of various alcohol concentration. The alcoholic strength of each liquid was determined by its specific gravity using a pycnometer. The bottles were tightly stoppered, placed in a reel with a capacity of 12 bottles, and immersed in a constant temperature bath. Here, they were rotated by a chain drive from a small gear-head motor at 25° for forty-eight hours. Clear solutions were discarded. Those which showed solid phase were considered to be saturated and were strained through cotton in a closed system. The sorbitol concentration was determined by the periodic acid titration method as previously mentioned. Results obtained were a weight-weight per cent. These were converted to weight-volume per cent by use of the specific gravity of the saturated solutions.

TABLE I

SOLUBILITY OF SORBITOL IN HYDROALCOHOLIC LIQUIDS AT 25° C.

Sample	% v/v C_2H_5OH	Specific Gravity of Saturated Solution	% w/w Sorbitol	% w/v Sorbitol
1	0	1.308	71.90	94.05
2	11.33	1.284	68.62	88.22
3	20.73	1.265	66.02	83.50
4	33.86	1.233	62.38	76.92
5	41.47	1.200	57.98	69.59
6	52.80	1.152	50.45	58.12
7	62.33	1.089	42.70	46.49
8	71.56	1.026	33.84	34.72
9	82.20	0.9123	13.64	12.42
10	90.94	0.8433	3.41	2.88
11	95.41	0.8177	1.92	1.57

Assay Procedure

Reagents—Sodium meta-periodate (G. Frederick Smith Chemical Company), 13.25 Gm./L. in distilled water with 75 ml. of sulfuric acid 1N; sodium arsenite 0.025N with sodium bicarbonate as a buffer; potassium iodide 10% w/v; starch indicator solution, 3 Gm. soluble-starch Merck reagent dissolved in 500 ml. distilled water and with 20 mg. of mercuric iodide as a preservative; sodium bicarbonate, Merck reagent, finely powdered.

Approximately 1-1.5 Gm. of each saturated solution was weighed accurately into a 250 ml. volumetric flask. The sample in the volumetric flask was then diluted to the mark. A 10 ml. aliquot was transferred to an Erlenmeyer flask and the alcohol was evaporated by allowing to simmer on a water bath for 15 minutes. To this was

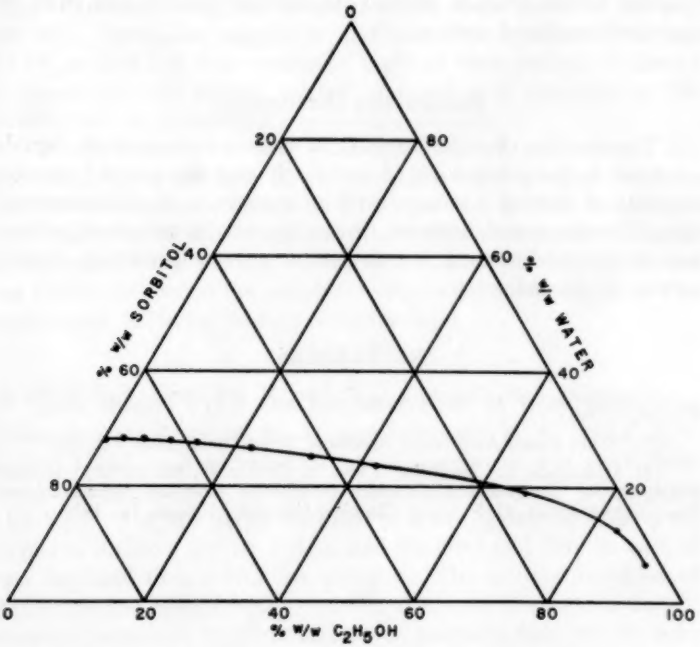

FIG. 2. PHASE DIAGRAM OF SORBITAL SOLUBILITY IN HYDROALCOHOLIC LIQUIDS AT 25° C.

then pipetted accurately 10 ml. of sodium periodate solution. The solution was heated to boiling, and cooled quickly to room temperature with running water. To this solution was then added an excess of sodium bicarbonate, followed by 10 ml. of potassium iodide solution. After the solution was allowed to stand for 3-5 minutes, the liberated iodine was titrated with 0.025N sodium arsenite solution using starch solution as the indicator. A blank titration was also run.

Calculations—The sorbitol concentration in the saturated solutions was calculated as follows:

$$\text{Weight \% Sorbitol} = \frac{25(\text{B-S})18.22 \times 100}{\text{wt. sample} \times 1000}$$

in which B = ml. sodium arsenite solution required for blank; S = ml. sodium arsenite solution required for sample; and 18.22 = equivalent weight of sorbitol (3).

Results and Discussions

The amounts of sorbitol soluble in various hydroalcoholic liquids are listed in Table I and Fig. 1 and 2. It may be observed that the solubility of sorbitol is reduced with an increase in alcohol concentration. The data reveal, however, that an appreciable amount of sorbitol may be dissolved in most pharmaceutical systems containing alcohol, such as elixirs and syrups.

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SELECTED ABSTRACTS

Neuropathy From Isoniazid Prevented By Pyridoxine. Carlson, H. B. et al. *New Eng. J. Med. 255:*118 (1956). Symptoms of peripheral neuropathy have been observed in a high proportion of patients receiving isoniazid. Higher doses of isoniazid were found to be associated with greater frequency and severity of this complication. A similar peripheral neuropathy has been induced in human beings by the administration of the pyridoxine antagonist, desoxypyridoxine. Studies have also shown that the administration of pyridoxine along with isoniazid did not interfere with the therapeutic effectiveness of the isoniazid.

The authors reported that 274 patients were treated for at least 2 months with 8 to 16 mg. of isoniazid per Kg. of body weight per day. Pyridoxine was also administered in doses of 25 to 200 mg. per day. Symptoms suggestive of neuropathy were noted in only 11 (4 per cent) of these patients. Eight of these patients continued to receive therapy without further progression of symptoms or the development of demonstrable neurologic changes.

In the majority of these patients 25 mg. of pyridoxine a day prevented the appearance of peripheral neuropathy when isoniazid was administered in a dosage of 8 mg. per Kg. of body weight per day. Likewise, 50 mg. of pyridoxine was effective when the isoniazid dosage was 16 mg. per Kg. Thus, it would appear that pyridoxine can effectively prevent the peripheral neuropathy frequently otherwise encountered following therapy with isoniazid.

Side Effects From the Administration of Ethylenediamine Tetra-Acetate. Perry, M. H., Jr., and Schroeder, H. A. *Am. J. Med. 22:*168 (1957.) A patient with amyloid nephrosis was given three series of intravenous injections of ethylenediamine tetra-acetate (EDTA). The first series consisted of 2 Gm. a day for 7 days, the second of 3 Gm. a day for 7 days, and the third of 3 Gm. on each of two days and then 4 Gm. for one day. The urinary excretion of cholesterol and several metals, namely, zinc, iron, manganese, copper, titanium, vanadium, molybdenum, silver, cadmium, lead and tin were determined.

There was a marked cholesterolytic effect following the administration of the EDTA as well as about a sixfold increase in the loss of zinc in the urine. To a lesser extent, iron and manganese were also found to be excreted to a higher degree. The excretion of the other metals was not increased. During the course of each series of injections, mucocutaneous lesions resembling acute avitaminosis B occurred. Upon withdrawal of the EDTA, the lesions cleared completely within a few days. The administration of 10 mg. of riboflavin, 250 mg. of nicotinamide, and 100 mg. of pyridoxine hydrochloride following the first series of injections probably aided in the clearing of mucocutaneous lesions. However, concurrently administered high vitamin supplements did not prevent the development of these lesions during the second course of therapy with EDTA.

Similar results were obtained in a second patient reported. The authors suggested that the lesions which developed may be associated with the high zinc loss in the urine.

Blood Concentrations of Two New Sulfonamides as Compared with Sulfadiazine. Foerster, D. K., Martin, W. J., McGuckin, W. F., and Nichols, D. R. *Proceed. Staff Meet. Mayo Clinic 31*:678 (1956). The disadvantage that sulfonamides must be administered every 4 to 6 hours to maintain therapeutic blood levels led to the development of the two new sulfonamide compounds used in this study, sulfaethylthiadiazole and sulfamethoxypyridazine. The blood levels obtained following oral administration were studied in the following manner. Seventeen subjects having no urinary obstruction or evidence of renal disease received 2 Gm. of sulfadiazine by mouth. Blood samples were taken 6, 12 and 24 hours thereafter. Forty-eight hours after the administration of sulfadiazine, the same 17 subjects and 5 additional ones received 2 Gm. of sulfaethylthiadiazole by mouth. Samples of blood were obtained 6, 12, 24, and 36 hours thereafter. Seventy-two hours after receiving the sulfaethylthiadiazole, 18 of the subjects received 2 Gm. of 3-sulfanilamido-6-methoxpyridazine by mouth. In these subjects samples of blood were obtained 6, 12, 24, 48 and 72 hours thereafter.

The mean blood level 6 hours after administration for sulfadiazine was 3.06 mg. per 100 ml., for sulfaethylthiadiazole was 6.05 mg., and for sulfamethoxypridazine was 7.85 mg. per 100 ml. After 24 hours

the mean blood levels were 1.2, 1.7, and 5.3, respectively. Detectable concentrations were present in the blood 36 hours after the administration of sulfaethylthiadiazole and 72 hours after administration of sulfamethoxypyridazine. Therefore, it is evident that the blood levels were higher and were maintained for longer periods following oral administration for both of the new sulfonamides as compared with sulfadiazine. Sulfamethoxypyridazine provided the highest blood levels for the longest period of time.

The Metabolic Effect of Intravenously Administered Emulsions. Levey, S., Krieger, H., Benson, J. W., Davis, J. H., and Abbott, W. E. *J. Lab. and Clin. Med. 49*:61 (1957). When it is necessary to feed a patient intravenously, particularly post-surgically, it is difficult to provide more than 1,500 to 1,800 calories per day by means of carbohydrates and amino acids alone. Since fat emulsions provide about 900 calories in 600 ml. of fluid, the administration of fat emulsions makes possible an increase in the caloric intake. The increase in caloric intake permits the administered nitrogen to be used for tissue fabrication.

Previous studies have shown that, following various types of trauma, patients go into a period where they develop large nitrogen deficits. For example, patients having had partial gastrectomies and maintained post-operatively on only intravenous hexose solutions, showed an average cumulative nitrogen deficit of 60 Gm. By increasing the caloric intake and nitrogen intake, a comparable group showed an average deficit of 30 to 35 Gm. Four patients reported in this study who had a subtotal gastrectomy and were maintained on protein hydrolysates, hexoses and fat emulsions showed a five-day nitrogen deficit of only 3 to 14 Gm. Two other patients with cancer of the esophagus and treated in this manner showed either a positive or a slightly negative nitrogen balance.

The authors, therefore, concluded that the large nitrogen deficit usually seen following surgical trauma seems to be mainly the result of poor post-operative nutrition rather than of a so-called stress reaction. They concluded that the intravenously administered fat emulsion increased the caloric intake to such an extent in these patients that there was an improved utilization of the protein hydrolysate with a decrease in the nitrogen deficit.

BOOK NOTICES AND REVIEWS

Heterocyclic Compounds, Vol. 3. Edited by Robert C. Elderfield. John Wiley and Sons, Inc., New York 16, N. Y., 1952. vi + 442 pp. Price $12.00.

Heterocyclic Compounds, Vol. 4. Edited by Robert C. Elderfield. John Wiley and Sons, Inc., New York 16, N. Y., 1952. vi + 674 pp. Prices $17.00.

It is natural to consider these two volumes together as it was originally intended to publish both in one volume. To do this would have made an unwieldy book of over one thousand pages. Volume 3 consists of five chapters dealing with the chemistry of: Indoles, Isoindoles (comprising over one-half the volume), Carbazole, Pyrindine, Quinindine and related compounds and Bicyclic system with a nitrogen atom common to both rings.

The fourth volume is devoted to the chemistry of Quinoline, Isoquinoline, the Acridines, Phenanthridine, and Benzoquinolines. Each of the chapters in both volumes is written by a prominent worker in his individual field. Very little is included on the alkaloids related to the heterocycles discussed, but many references to treatise articles have been included. Both volumes are of considerable importance to the pharmaceutical chemist due to the large number of medicinals possessing a nitrogen heterocyclic nucleus.

A. R. GENNARO

Heterocyclic Compounds, Vol. 5. Edited by Robert C. Elderfield. John Wiley and Sons, Inc., New York 16, N. Y. 1957. vi — 744 pp. Price $20.00.

Volume 5 of this well known work considers the chemistry of the five membered heterocycles containing two hetero atoms and their benzo derivatives. Specifically discussed are; 1,3-Dioxolane and derivatives, Pyrazoles and related compounds, Indazoles, Imidazoles, Oxazoles, Benzoxazoles and related systems, Isoxazoles and Thiazoles. The four previous volumes suffered somewhat from the meager index

provided and the editor states in the preface that a "more comprehensive" index has been assembled for this volume. It is the opinion of the reviewer that the preceding volumes had little more than an enlarged table of contents. In this book only twenty one pages are devoted to an index. This is much too short for a text of 722 pages containing such a wealth of valuable information. The index is still in need of improvement.

As in the former editions, this volume contains a great deal of information gleaned from the voluminous literature on the heterocyclic compounds. The literature appears to be covered through 1955. Regardless of the shortcomings of the index this book is still a must for any organic chemistry library.

A. R. GENNARO

Practical Dermatology. By S. M. Peck and L. L. Palitz. 380 pp. McGraw-Hill Book Company, Inc., New York, N. Y., 1956. Price $7.00.

This text has been prepared by the authors to serve as a survey of dermatological disorders for the general practitioner. A thorough and complete discussion of dermatological diseases—their etiology, pathologic-physiology, and therapy—are presented in a very practical manner. The therapeutic suggestions of the authors are based solely on their experience in the treatment of dermatological diseases and, in many cases, it is evident that they are not in agreement with other practitioners in their field.

The text is well suited for the busy practitioner, for whom it is intended. The illustrations of specific diseases, which are presented in each chapter, are excellent and should aid the general practitioner in diagnosing dermatological conditions as they present themselves in office practice.

The section of each chapter on treatment is also of value to the general practitioner. The major criticism of this work is the poor treatment given the antibiotics. Little mention is made of the topically-used antibiotics and there is practically no discussion of antibiotic spectrum in the treatment of dermatological diseases known to be caused by pathogenic microorganisms.

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